بسم الله الرحمن الرحيم

عنوان المحاضرة: Choriocarcinoma

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Definition:

It is a malignant tumor of the chorion; i.e. it's a trophoblastic disease so it doesn't arise from the uterus itself but present within it

Incidence: varies acc. to geographic distribution

Most common in Southeast Asia (as Vesicular mole), Rare in western countries 1:14000,

Higher in Females with blood group B whose partner is blood group A or AB

Etiology: malignant transformation of vesicular mole due to decreased body immunity against trophoblastic vascular invasion

Types:

A) Gestational: (has a relation to pregnancy)

Follows vesicular mole (50%), abortion (25%), full term baby (22.5%) or ectopic pregnancy (2.5%)

B) Non Gestational: (not related to pregnancy)

It is a germ cell tumor of the ovary

Pathology:

A) Macroscopically:

1-Dark, Red, Hemorrhagic & Necrotic lesion which may be:

- Localized: circumscribed nodule in the fundus
- Polypoidal: Polyps of malignancy within the uterus
- Diffuse (infiltrative)
- Intramural: Inside the wall (myometrium) resembles fibroid, most dangerous as it is asymptomatic (no bleeding) and gives negative results in D&C biopsy

2-Enlarged ovaries with Theca-lutein cyst

B) Microscopic:

1-Islands of trophoblastic tissues among lakes of blood spaces

2-Invasion of uterine muscle wall + ischemia & necrosis

**It's the only tumor in which we don't depend upon the cytological criteria of malignancy of the cell for diagnosis of malignancy, but depend on the "Avillous Pattern" (i.e. No intact villi) → Pathognomonic

C) Mechanism of Spread:

1-Local: to the surroundings (myometrium, fallopian tubes, ovaries, adnexa, bladder, rectum)

2-Lymphatic: according to the site of malignancy (as endometrial/cervical carcinoma)

e.g.: -Fundus/body→ internal iliac → common iliac → para-aortic LNs

-Isthmus/cervix→ external iliac → common iliac → para-aortic LNs

3-Hematogenous: occurs early (esp. to the lungs → so presented by hemoptysis)

D) Staging: (FIGO /ISSTD)

Stage I	Malignancy confined to the uterus
Stage II	Extends outside the uterus but is limited to the genital structures (adnexa, tubes, ovaries, parametrium)
Stage III	extends to the lungs
Stage IV	Any secondary organ metastasis

*FIGO = International Federation of Gynecology and Obstetrics

*ISSTD = International Society for the Study of Trophoblastic Diseases

**** Grading (Risk Factor Score): "WHO"**

2 Risk Factors:

1-Level of serum hCG > 100,000 mIU/mL

2-Disease duration > 6 months after termination of pregnancy

Grade A	**No Risk factors**
Grade B	**One Risk factor**
Grade C	**Both Risk factors**

E) Complications

i) General complications of malignancy:

1-Cachexia 2-Hemorrhage 3-Infections 4-Intestinal obstruction 5-DVT, Pulmonary embolism

ii) Complications of vesicular mole:

►General: 1-Hyperemesis Gravidarum 2-Pregnancy induced hypertension 3-Thyrotoxicosis 4-DIC 5-Amniotic fluid embolism 6-ARDS

►Local: 1-Invasion→ massive bleeding 2-Perforation 3-Infection 4-Theca lutein cyst torsion, rupture or hemorrhage

iii) Specific complications of choriocarcinoma: (d.t. spread)

1-Liver: metastatic nodules → rupture→ acute abdomen

2-Brain: thrombotic manifestations, Hemiplegia

►Cause of death: Local complications (severe hemorrhage & infections)

*****In: Ovarian CA→ Intestinal obstruction, Cervical CA → Renal failure, Endometrial CA → Peritonitis***

Management:

A) Symptoms:

1-History of recent termination of (ectopic pregnancy, vesicular mole) followed by:

"Secondary post-partum/post-abortive hemorrhage"

●●*Rule:* Any patient with: ●Secondary postpartum/postabortive hemorrhage ●Ecopic pregnancy

➔ Should undergo D&C with histopathology to exclude Choriocarcinoma

2-Level (↑titre) of hCG (during proper follow-up of a case of vesicular mole) (may be non-secretory but rare)

3-Bad general condition, cachexia, very offensive vaginal discharge, anemia that cannot be attributed to vaginal bleeding

4-Symptoms of metastasis: e.g. Lung: hemoptysis, chest pain, cough & pulmonary hypertension

5-Symptoms of complications: e.g. rupture liver nodule→ Acute abdomen & internal hemorrhage

B) Signs:

►General: 1-Pale, cachexia 2-Chest: crepitations 3-Signs of thyrotoxicosis 4-Signs of hypertension 5-Jaundice 6-Vircow's LNs

►Abdominal: 1-Pelvi-abdominal mass 2-Heptomegally, liver nodule 3-Ascites 4-Para-aortic LNs

►Pelvic:

1-Vulval/vaginal nodules (esp. suburethral area & at fornices) **Don't excise before proper diagnosis

2-Pelviabdominal mass firm to hard (enlarged uterus) 3-Adenxal mass (Theca lutein cysts in the ovaries)

C) Differential Diagnosis:

1-Any case of secondary postpartum/postabortive hemorrhage should be considered choriocarcinoma untill proved otherwise

2-Ectopic pregnancy 3-Bleeding in any site of the body

D) Investigations

i) To Screen: 1-Proper follow-up for all cases of vesicular mole (hCG, CXR, US, Examination, ...)

2-Histopathology for all cases of 2ry postpartum/postabortive hge & ectopic pregnancy

ii) To Confirm diagnosis:

1- β-hCG levels: extremely high 2- D&C biopsy & histo-pathological examination → avillous pattern

iii) To Certify spread:

Imaging: 1-US, CT, MRI on female genital tract

2-CXR (Cannonball appearance), Lung CT & MRI 3-Liver US, CT

E) Treatment

i) Prophylactic: "Proper Screening"

ii) Active:

1-Chemotherapy: (95% of cases)   2-Surgery: (5% of cases)

Depend on: (Staging / Grading / Patient desire for further fertility)

1-Chemotherapy: (95% of cases)   2-Surgery: (5% of cases)

Stage 1: **(low risk)**

a) Want to preserve the uterus:

1-Single agent chemotherapy (e.g. Methotrexate 1mg/kg body weight alternative with folinic acid)

2-If No improve→ combined Chemo (Methotrexate + Actinomycin D or 5-Chlorouracil or Nitroprusside)

3-If No improve → search by (US/CT/Doppler) for focal lesion & resect it then chemotherapy

b) Doesn't want to preserve uterus & had completed her family:

→ Single agent chemotherapy then Hysterectomy (total/pan) then single agent chemotherapy again

****After single agent course, follow up level of hCG weekly till it is negative for 3 weeks, then every month for one year during which patient administers Combined OCPs**

****Patient can get pregnant after this year, and there is NO increased risk of abortion or fetal malformations or GTN (gestational trophoplastic neoplasia)**

Stage 2: **usually low risk: as Stage 1**

Stage 3: **usually high risk so start with combined chemotherapy and follow up will be for 2 years**

Stage 4: Aggressive chemotherapy "CHAMOCA protocol"

(Cyclophosphamide, Hydroxyurea, Actinomycin D, Methotrexate, Oncovin. Ca^{2+} leucovorin, Adriamycin)

Prognosis of choriocarcinoma is good:

●Stage 1 – 2 → 100% survival rate

●Stage 3 – 4 → 75% survival rate
